

From: Kaushal, Sumesh
Sent: Tuesday, August 12, 2003 4:46 PM
To: Li, Janice; Kelly, Robert; Crouch, Deborah; Falk, Anne; Bertoglio, Valarie; Wehbe, Anne Marie; Weitach, Joseph; Nguyen, Quang (AU1632); Shukla, Ram; Schnizer, Richard; Priebe, Scott; Ton, Thaian; Qian, Celine; Nguyen, Dave; Reynolds, Deborah; Martinell, James; Angell, Jon E; Wilson, Michael; Kaushal, Sumesh; Epps-Ford, Janet; Guzo, David; Katcheves, Konstantina; Ketter, James; Leffers, Gerald; Loeb, Bronwen; McKelvey, Terry; Sandals, William; Yucel, Irem; Epps-Ford, Janet; Lacourciere, Karen; McGarry, Sean; Zara, Jane; Sullivan, Daniel; Nguyen, Dave
Subject: BAVAP#09042488

Ready to allow:

A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to a response element wherein said modified ecdysone receptor comprises:

- (a) a ligand binding domain that binds to an ecdystroid,
- (b) a DNA-binding domain obtained from a DNA-binding protein, which binds to said response element; and
- (c) an activation domain of a transcription factor,

wherein at least one of said DNA-binding domain or said activation domain is not obtained from a native ecdysone receptor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein; and

(ii) a DNA construct comprising said exogenous gene under the control of said response element, wherein said response element:

- (a) is a modified response element which comprises, a first half-site and a second half-site separated by a spacer of 0-5 nucleotides; and wherein said second half-site is obtained from a glucocorticoid receptor subfamily response element
- (b) binds to said modified ecdysone receptor, and
- (c) does not bind to Farnesoid-X receptor (FXR);

said method comprising providing to the cell an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

Title: METHOD FOR MODULATING EXPRESSION OF EXOGENOUS GENES IN MAMMALIAN SYSTEMS, AND PRODUCTS RELATED THERETO

Inventor: EVANS, RONALD M.

Priority: 04/05/96

Related patents: 5874534, 6576422, 62245531

S. Kaushal

CM1 12A07 AU1636

Ph: 703-305-6838

Mail Box: 11E12